UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,265	09/16/2003	Edith Mathiowitz	19141-546 DIV3 CON2	1449

23579 7590 04/18/2006

PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE
SUITE 1200
ATLANTA, GA 30361

EXAMINER	
LEAVITT, MARIA GOMEZ	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,265	MATHIOWITZ ET AL.	
	Examiner	Art Unit	
	Maria Leavitt	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02-17-2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Applicant called the Examiner on April 3, 2006, to bring to her attention that the IDS filed on 02-02-2006 were not properly considered in the Final Rejection in view of issue Patent US 6,262,034 . Additionallly, Applicant pointed out that rejections under Obviousness Type Double Patenting-No secondary reference(s) did not comply with the law for ODP rejection.
The Examimer agreed to reexamine the case and to make corrections as needed and invited Lawyer Pabst to contact the examiner sepervisor, Dave Nguyen fot any further concerns .

Detailed Action

1. Applicant called the Examiner on April 3, 2006, to bring to her attention that the IDS filed on 02-02-2006 were not properly considered in the Final Rejection in view of issue Patent US 6,262,034 . Additionallly, Applicant pointed out that rejections under Obviousness Type Double Patenting-No secondary reference(s) did not complied with the law for ODP rejection. The Examimer agreed to reexamine the case and to make corrections as needed .
2. Applicant's request for reconsideration of the finality of the rejection of the last Office action, and further in view of the last Office Action of record, is persuasive and, therefore, the finality of that action is withdrawn.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. Status of claims. The specification has been amended; claims 3-17 have been amended and claim 18 has been cancelled by amendment dated February 17, 2006.

Response to arguments

Withdrawn rejections in response to Applicant arguments or amendments

In response to Applicant's amendment of the word "system " by the word "composition" in claims 3-14, the examiner has considered the argument persuasive.

In response to Applicant's amendment of the word "naked DNA " by the word "gene" in claims 3, 8, 9, 10, 11, 14, and 15, the examiner has considered the argument persuasive.

In response to Applicant's amendment of the phrase "consisting of stents, coating, slabs, and films " by the phrase "in the form of a stents, coating, slabs, gels and films" in claim 3, the Examiner has considered the argument persuasive.

Rejections under 35 U.S.C. 102

Rejections under 102 over U.S. Patent No. 5,639,473 to Grinstaff et al., or U.S. Patent No. 5,763,416 to Bonadio et al., have been withdrawn in view of the attached Declaration under 37 C.F. R. 1.131.

Rejections under 102 over Tice and al., has been withdraw as the Examiner has considered Applicants arguments persuasive.

Rejections under 35 U.S.C. 103

Rejections under 103 over US. Patent No 5,770,580 to Ledley in combination with Grinstaff et al., or Bonadio and al., has been withdrawn as the Examiner has considered Applicants arguments persuasive.

Remaining rejections in response to Applicant arguments or amendments

35 U.S.C. 112, first paragraph, written

Claim 17 remains rejected udder 35 U.S.C. 112, first paragraph.

In response to applicant's assertion (Remarks, p. 4) that Claim 17 recites the limitation,

" the polymeric matrix is formed after implantation into the mammalian subject" which finds not writing support from the as-filed application, the comment is not found persuasive.

As indicated in the previous Office action, the closest reference as to the way of polymerizing the monomers and DNA into a polymer after implantation, is be UV light *in vivo* without damaging the DNA in the subject. Applicant states that the system referred to on page 13, line 18, is a diacrylated-poly(lactide-co-glycolide)-PEG polymer that is FDA approved. It is not clear how results of lack of DNA damage in a polymer crosslinked by UV light without containing DNA, can be extrapolated to an *in vivo* system wherein the polymer comprises DNA and UV light is contemplated to be applied to form the polymer after implantation. Further, the Declaration under 37 C. F. R. 1.131 supports the formation of a polymer precipitate with DNA which is implanted as DNA/PLA pellets in the left and right legs of the incised rat muscles, thus the polymer is formed before implantation. Hence the statement on page 13 that this process can be carried *in vitro* as well *as in vivo* does not address the formation of the polymeric matrix after implantation into the mammalian subject. Further, there are not *in vivo* working examples present in the as-filed application that provides any factual evidence drawn to polymerization of a matrix after implantation. Hence, rejection of claim 17 is maintained.

Claim Rejections - 35 USC § 102e

The following is a quotation of the appropriated paragraphs of 35 U.S.C. 102 that forms the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless:

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraph (1), (2) and (4) of section371© of this title before the I invention thereof by the applicant for patent.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-7, 9-13 and 15-17 are rejected under 435 U.S.C. 102(e) as being unpatentable over Ledley et al., (US Patent No. 5,770,580, filing date May 30, 1995).

Claim 3 of the instant application is interpreted as a composition for gene delivery, the composition comprising a polymeric matrix and a DNA dispersed within the polymeric matrix. The dispersed amount of DNA when given the broadest possible interpretation is considered as an amount of DNA encoding a protein that is effectively expressed so as to provide a therapeutic effect. Ledley et al., teach a method for gene delivery (e.g., release) and transient gene expression comprising the steps of administering formulated DNA expression vectors to cells associated with fluid spaces *in vivo* under conditions in which cells associated with the fluid space incorporate the formulated DNA expression vector (abstract, and claim1). Ledley et al., disclose that the method has been able to achieve significant levels of expression by directly injecting formulated DNA vectors into cells associated with fluid spaces (e.g., joints, thyroid, ear and eye) and express recombinant genes at levels comparable to levels seen in muscle (column 6, lines 13-16). Ledley et al., further teach that the method allows use of genes as medicines that can be administered intermittently in response to acute disease or over the long term to establish

steady state levels of a therapeutic gene product, and thus, genes can be used in clinical practice (column 6, lines 35-41). Ledley et al., disclose *in vivo* cells and tissues affected by the gene transfer method, e.g., synovial cells, chondrocytes , extracellular matrix or cartilage, bone, periosteum of bone, inflammatory cells resulting from inflammatory processes, lymphocytes, mast cells, monocytes, eosinophils, fibroblasts (column 7, lines 40-55), and cells associated with enhancement of repair, regeneration, and recovery of essential structures of the joint (column 16, last paragraph). More specifically, Ledley teaches that the formulated DNA expression vectors with formulated elements include gels, slow release matrices soluble or insoluble particles, as well as other formulation elements not listed (col. 8, lines 42-47; col. 14, lines 10-15; col. 35, lines 15-21) which enhance the delivery, uptake, stability, and expression of genetic material into cells . Genes employed in the method of Ledley include genes encoding collagens, extracellular matrix proteins, IL-1, IL-4, growth factors, enzymes for synthesis and secretion of synovial fluid, hormones, receptors and cytokines (paragraph bridging column 9 and 10).

Thus, Ledley teaches all the claimed limitations and Anticipates Applicant's claimed invention.

Rejection, Obviousness Type Double Patenting-No secondary Reference(s)

Claims 3-17 remain rejected under the judicially created doctrine of obviousness-type double patenting over claims 1 and 2 of U. S. Patent No. 6,620,617, filing date March 23, 2001; over claims 1-8 of U. S. Patent No. 6,475,779, filing date Oct. 15, 1998 and over claims 1-14 of U. S. Patent No. 6,262,034, filing date Nov. 25, 1997, in view of over Ledley et al., (US Patent No. 5,770,580, filing date May 30, 1995).

Claims in U. S. Patent No. 6,620,617, U. S. Patent No. 6,475,779 and U. S. Patent No. 6,262,034, are drawn to microparticles comprising a synthetic, biocompatible, non-degradable polymeric matrix and an effective amount of DNA contained within the matrix. Further, said DNA is released after implantation into a subject for a therapeutic treatment.

Ledley et al., a method that allows use of genes as medicines that can be administered intermittently in response to acute disease or over the long term to establish steady state levels of a therapeutic gene product, and thus, genes can be used in clinical practice (column 6, lines 35-41). Ledley further discloses that formulated DNA expression vectors with formulated elements include gels, slow release matrices soluble or insoluble particles, as well as other formulation elements not listed (col. 8, lines 42-47; col. 14, lines 10-15; col. 35, lines 15-21) which enhance the delivery, uptake, stability, and expression of genetic material into cells.

It would have been obvious for one of ordinary skill in the art to use microparticles in the form of gels, exemplified in the Ledley reference, for obtaining efficient introduction of exogenous genes into a patient. Additionally it would have been obvious in view of the contemplated definition of matrix in the as filed specification in the form of a microparticle such as a microsphere or microcapsule and forms such as films, coatings, gels, implants, and stents (p. 5, lines 16-22)

Thus, Claims 3-17 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U. S. Patent No. 6,620,617, filing date March 23, 2001; over claims 1-8 of U. S. Patent No. 6,475,779, filing date Oct. 15, 1998 and over claims 1-14 of U. S. Patent No. 6,262,034, filing date Nov. 25, 1997, in view of Ledley et al., for the reasons of record.

New Grounds of Rejection

Claim Rejections - 35 USC § 112- First paragraph- New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3 recites the limitation "loaded into the polymeric matrix at a concentration between about 0.01 and 90% and is". The specification discloses on p. 22, lines 9-19, that 100 ul of either circular or linear DNA (between 1 and 2 mg/ml diluted 1:5 in buffer) was introduced into the aliquots containing the mixtures of 1 g PLA and 2 g PLA that has been dissolved in 10 ml of methylene chloride and 5 drops of Span 85. No other teachings are anticipated about the encapsulation of linear and supercoiled DNA in a PLA blend. Thus is not clear that the

Applicant was in possession of a genus of undefined polymeric matrix at a concentration between about 0.01 and 90% at the time of filing.

Claim 3 will remains rejected until Applicant cancels all new matter.

Claim Objections

Claim 15 is objected to as being dependent upon claim 4 and reciting the term "system" which is not found in claim 4.

Conclusion

Applicant response file on February 17, 2006 has been considered by the Examiner but is moot in view of the new grounds of the rejection, which is necessitated by the claims amendment.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nguyen Dave can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria Leavitt, PhD
Patent Examiner P/1633
Remsen 2B55
Phone: 571-272-1085
Email: maria.leavitt@uspto.gov

JANET L. EPPS-FORD, PH.D.
PRIMARY EXAMINER